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NEW DATA ON THE FUNCTIONAL BIOCHEMISTRY OF THE BRAIN

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One of the most important tasks of biological chemistry is to discover the chemical processes lying at the base of a specific function of a given organ. In this connection, the functional biochemistry of the brain is particularly important. Disclosing the biochemical nature of irritability and inhibition, the chief nervous processes, will help us to understand more deeply the essence of these processes and to be guided in exerting influence upon them.

Many studies have been done by Soviet and foreign scientists in the field of the functional biochemistry of the brain. In our country this branch of biochemistry is successfully developing, thanks to the investigations of A. V. Palladin and his associates, and those of groups of scientists under the direction of G. Ye. Vladimirov, Ye. M. Kreps, Kh. S. Koshtoyants, and others.

In spite of numerous experiments, many problems related to the biochemical nature of the functional conditions of the brain still remain unexplored. This is explained by the fact that an experimenter working on the problems of the functional biochemistry of the brain must create the conditions necessary for normal operation of the brain, and this entails many difficulties. In experiments in vitro, even when the conditions necessary for the test are strictly maintained, the brain tissue undergoes a number of changes. Modern experimental techniques do not make it possible to discover in vitro the processes lying at the base of irritability and inhibition. Besides, in studying the problems of the relation between the metabolism of the brain and its function, a biochemist must have a developed criterion as regards the physiological manifestations of this function and of the strength and duration of irritability and inhibition.

A specific chemical topography is of no small importance, as are the characteristics of metabolism in the different parts of the brain. It is known that various agents react unequally on metabolism in different parts of the central nervous system. In addition, it is necessary to consider the specific properties of the stimulus applied and its effect on the metabolism in cerebral tissue, as various stimulants and narcotics produce an unequal effect on the metabolism of the brain. It should be

borne in mind that the brain has insignificant sources of energy and that its functional activity is connected with a great expenditure of energy, the chief source of which is the glucose carried in the blood. Therefore, in working out problems related to the functional biochemistry of the brain, we should take into account the relation existing between the metabolism of the brain and the effector organs. The brain, being an organ securing the delicate regulation of metabolism in the effector organs, receives corresponding nutritive substances and thereby assures its own function. The effector organs functioning against a specific background cannot but reflect on the metabolism of the brain and, thereby, on its functioning. The incomplete list of problems given above indicates that many difficulties confront research workers and explains the contradictory data presented by authors in this field.

In studying the metabolism of the brain during irritability and inhibition, many research workers effected these functional conditions by using various pharmacological agents or electric stimuli. This cannot be considered as an adequate method for disclosing the true picture of the processes characterizing the functioning of a normal brain. In this connection, the research conducted on the whole organism with the conditioned-reflex method is of interest. This method is the most physiological and permits us to determine the processes which occur in the brain when the cortex is stimulated or inhibited. Experiments of Soviet scientists in this field stand out prominently.

According to numerous literary data, an increased functional activity of the brain is accompanied by the utilization of large quantities of glucose and oxygen. The breaking down of glycogen for the most part of free adenosine triphosphate and creatine phosphate occurs in the cerebral tissue under the influence of various stimulating agents. The quantity of lactic acid, inorganic phosphorus, and ammonia increases. Due to the separation of potassium ions and to the absorption of sodium ions, the correlation between the ion content of potassium and sodium changes. This occurs at the beginning of irritability and is of vital importance in the conductivity of nervous impulses. Many existing data indicate that there is an increase in the metabolism of proteins, ribonucleic acid, phospholipids, and lipoproteins. In the process of irritation, the metabolism of these substances in the nerve cell increases in relation to the nerve activity. Irritation caused by different means results in the liberation and breaking down of neurohumoral materials--acetylcholine, serotonin, and noradrenalin. Spasms of different origin cause an increase in the quantity of gamma-aminobutyric acid; this is thought to be significant in bringing about the process of inhibition.

However, considerable fluctuation and, frquently, opposite changes can be observed in the processes described above, depending on the character of the stimulus used, its dose and duration. The effect of stimulation on different parts of the brain and on the nerve cells is also unequal.

The data given indicate that an increase in the functional activity of the brain is connected with an increase in the metabolism of carbohydrates, proteins, nucleic acids, phosphotides, neurohumoral and mineral substances, etc. But the question of which primary process lies at the base of irritation, and of which biochemical processes are secondary, remains unexplained.

The nervous system uses a number of substances as sources of energy for its functioning, in particular, glucose, oxydolysis of which is accompanied by the formation of macroergetic compounds mainly adenosine triphosphate acid (ATP). ATP plays an important role in glycolysis and in the formation of glutamine, nucleotides and nucleic acids, phospholipids, phosphoproteins, and, finally, acetylcholine. Acetylcholine is the most important mediator in the transmission of nervous excitation.

An oxidizing phosphorylation with the formation of ATP is necessary for overcoming the concentration gradient and preserving glutamic acid, gamma-aminobutyric acid, and potassium ions in the nervous tissue. This is also necessary for obtaining a selective permeability of the cellular membrane to the ions of potassium and sodium in order to displace the equilibrium between them, which is very important in the transmission of a nerve impulse. The energy of metabolism plays an exceptionally important role in the mechanism for maintaining a high intracellular concentration of potassium ions and a low concentration of sodium ions characteristic of a stimulated tissue. Thus ATP plays a versatile role in the metabolism of the nervous tissue and is very important for its function. However, we have yet to discover the effect of ATP on the irritated substance of the nerve cell, the function of the membrane in relation to the various mechanisms lying at the base of its selective permeability to the ions of potassium and sodium, and the processes of the formation and function of other neurohumoral substances, such as moradrenalin and serotonin.

Acetylcholine, noradrenalin, and serotonin are found in the nervous tissue mainly in a combined form. Under the influence of various irritants they are released; this is very important in the execution of the functional activity of the brain. When the inhibitory process develops, they become combined with proteins. The mechanism of the fixation and liberation of these neurohumoral substances remains unexplained. One of the main questions as regards the role of biochemical processes in a nervous function is the changes of protein substances in irritating and inhibitory processes. A number of scientists have demonstrated that metabolism of the brain proteins increases in irritation and, on the contrary, decreases in inhibition. But what change does the protein molecule undergo? Our information is very poor along this line.

The following studies in this field merit attention:

-- D. N. Nasonov and co-workers in connection with the reversible denaturation of proteins in irritation.

-- Kh. S. Koshtoyants on the role of the sulhydryl group of proteins in realizing the effect of nervous irritation and the action of acetylcholine.

-- A. L. Shabadash on changes in nucleoproteins in irritation and inhibition.

-- G. Ungar on changes in the structure of soluble proteins of the brain resulting from its increased activity.

-- G. M. Frank on the increased viscosity and changes in the dispersion of proteins in the nerve in irritation.

We should note that the energy required for the nervous activity of conducting impulses is very small in comparison with that needed for restoration. Compared with the blood, the nerve cells contain considerably more potassium ions and less sodium ions. A rapid release of potassium ions and fixation of sodium ions occur in the first phase of irritation. This process does not involve a big expenditure of energy, since it takes place in accordance with the concentration gradient.

The second phase is characterized by the absorption of potassium ions and the release of sodium ions, i.e., this process takes place against the concentration gradient. This involves a considerable consumption of energy, the main source of which is ATP. Glutinic acid plays an important role in the absorption of potassium ions by the nerve cells and the conservation of their concentration gradient.

In the first phase, the system of acetylcholine plays a leading role. In the nervous system it has as its specific function the transmitting of impulses in distinction to the other tissues, where there is also an unequal distribution of potassium and sodium ions. In the second phase, acetylcholine is synthesized once more with the participation of ATP and in the process of acetylation. The problem of the selective diffusion of potassium and sodium ions have not been sufficiently explored. Kh. Yussing, R. Keynes, and others indicate that the release of sodium ions and the absorption of potassium ions are brought about by different mechanisms.

Many experiments were conducted with a view to studying metabolism in the brain while its functional activity remained depressed. The majority of these experiments were devoted to finding out the effect of various narcotics on separate metabolic processes. There is no unanimous opinion concerning the mechanism of the effect of narcotics. Giving rise to one and the same external effect, various narcotic substances produce an unequal effect on the metabolism of the brain. Besides, the effect of narcotics changes in relation to their dose and length of use. In his report at the Fourth International Biochemistry Congress, Dzh. Kvostel developed a thought which he had expressed earlier on the basis of medical data and the results obtained in his laboratory. He thinks that narcotics and sedatives produce a double effect when given in low pharmacological

doses: 1) dissosiation between the processes of oxidation and phosphorylation, that is, a break in the oxidizing phosphorylation and the formation of ATP (this subsequently leads to a decreased absorption of oxygen by the cerebral tissue; 2) depression in the respiration of neurons, which was preliminary stimulated by the addition of potassium ions to the incubation media.

Potassium ion, besides stimulating respiration and glycolysis, also contribute to such amino acids, important for the nervous tissue, as glutamine, and aspartic and gamma-aminobutyric.acids. However, not all narcotics disturb the process of oxidizing phosphorylation as, for instance, alcohol, morphine, and others.

On the basis of experimental data, Dzh. Kvostel expressed his opinion that narcotics combine with lecithin, a component of the phospholipids of mitochondria. In this connection the structure of mitochondria breaks down, and as a result there is oxidizing phosphorylation, which takes place with the direct participation of mitochondria. This concept is definitely related to Overton-Meyer's hypothesis on the mechanism of the effect of narcotics.

Dzh. Kvostel and other scientists obtained the data of their investigations on narcotics from brain sections. Those data are undoubtedly of some interest but cannot be fully applicable to the whole organism. It is known that some narcotics produce one effect in vitro and another in vivo, which frequently can be quite an opposite effect. The question of which process is the initial one in the general picture of the narcotic's effect remains unclear.

The research of A. V. Palladin and co-workers is particularly interesting. They have established that in sleep induced by amytal an active metabolism of nucleic acids and carbohydrates occurs, there are changes in the activity of a number of ferments, and an increase in the content of ATP and a strengthening of synthetic processes take place in the brain. According to D. Rikhter and G. Grossland, there is an accelerated breaking down of acetylcholine in an increased activity of the brain. By contrast, sleep and anesthesia bring about an increase in content of acetylcholine of the brain. Ye. A. Vladimirova has demonstrated in her experiments that unconditioned and conditioned reflexes produce a marked rise in the content of ammonia (urethan) in the brain. On the other hand, protective and conditioned inhibition produce a marked reduction in the content of ammonia. We established an analogous mechanism in our laboratory. Thus in inhibition, active processes take place in the metabolism of the brain; they proceed in an opposite direction and condition the restoration of the work capacity of the nerve cells depleted during the period of irritation. These facts confirm Pavlov's thesis concerning the protective role of inhibition.

In recent years, interesting data were obtained regarding the substances constituting the brain and producing an inhibitory effect on its activity. This concerns mainly gamma-aminobutyric acid, which is formed in the brain from glutinic acid by decarboxylation and is found there in

large concentrations. Among all the amino acids of the cerebral tissue, only glutinic and aspartic acids surpass gamma-aminobutyric acid in their quantity. K. Eliott devoted his report at the Fourth International Biochemistry Congress (discussed at the symposium on biochemistry of the central nervous system) to the metabolism and inhibitory effect of gamma-aminobutyric acid. He was able to establish in his laboratory, in 1956, that the inhibiting reaction of cerebral extracts from mammals on nervous activity was secured by the gamma-aminobutyric acid present in the extracts. T. Khayashi and co-workers have demonstrated at the same time that gamma-aminobutyric acid and, in particular, gamma-aminobeta-hydroxybutyric acid, produce an inhibitory effect on the spasms induced by electric and chemical irritants. This discovery induced many scientists to conduct experiments. In various laboratories, the results obtained confirmed that gamma-aminobutyric acid is an important inhibitory agent and is essential for the functional activity of the brain. The mechanism of the action of gamma-aminobutyric acid still remains to be explored. At present we have indications that, besides this substance, a number of related compounds produce an inhibitory effect, in particular, gamma-amino-beta-hydroxybutyric acid. The presence of specific compounds in the cerebral tissue proves once more that the inhibitory process has an active character. We should study more extensively the inter-relation between the metabolism of these substances and other neurohumoral substances under different functional conditions of the brain.

In recent years, the question of the functional connection between the cells and neurons of neuroglia, which fills a considerable part of the cerebral tissue, became of a particular interest, owing to the experiments of H. Hiden and co-workers.

In his report at the Fourth International Biochemistry Congress, H. Hiden presented a number of data illustrating the high level of the metabolism and, in particular, of the oxidizing processes in individual cells of the neuroglia he isolated by a special method. From a number of indexes, such as respiration and amino acids metabolism, he demonstrated that the metabolism of glia cells surpassed that of nerve cells. On the basis of the results obtained in his laboratory and by other experimenters, H. Hiden stresses the significance of glia cells in the mechanism of transporting substances through the hematoencephalic barrier. He advances a hypothesis according to which a nerve cell with its surrounding glia cells functions as a single system. In his opinion, the glia cells produce substrates which are used by the nerve cells as a source of energy. In other words, the cells of neuroglia serve as energy suppliers for the neurons. Therefore, psychic disturbances may occur not only in the presence of the affection of neurons but also that of the cells of neuroglia.

In working on problems related to the functional biochemistry of the brain, we should have in view not only the functional interrelation between the glia cells and neurons, but also the reversible connection existing between the brain and effector organs. Thus, for instance, the

liver is the chief supplier of glucose, which is so important for the activity of the brain. The liver's production of glycogen is regulated by the nervous system. On the other hand, A. Geyger has demonstrated in his experiments that, in addition to glucose, the liver secretes cytidine and uridin, substances which help to transport glucose from the blood into the brain. There is no doubt but that in an intact organism, the functional activity of the brain is maintained by the activity of the effector organs. On the other hand, the brain is an important regulator of their function. There is no question but that it is important to discover the interrelation between the activity of the brain, the function of the effector organs, and their basic metabolism. From the above it follows that the regulation of metabolism by the central nervous system particularly by the cerebral cortex, is an integral part of the functional biochemistry of the brain.

Experiments along this line conducted by a group of our scientists (Division of Biochemistry, Academy of Sciences Armenian SSR; Department of Biochemistry, Yerevan Medical Institute) involved the use of various stimuli without conditioned reflex. It was demonstrated in the experiments on dogs that the irritation conditioned by adrenalin produces an increase in the level of glucose, ascorbic acid, and pyruvate (E. Ye. Mkheyan); of adrenalin-like substances (N. A. Yesayan); of calcium ions, fibrinogen, and prothrombin and in the activity of protease of the blood (K. G. Karagezyan). At the same time, the content of histamine decreased and the time of blood-clotting shortened. After a repeated administration of insulin there developed a conditioned hypoglycemia [see Note], a conditioned increase in the quantity of restored glutathione, and a reduction in the inorganic phosphorus of the blood (G. T. Adunts, V. B. Yegyan, and A. S. Oganesyan).

[Note.] S. G. Genes did not observe insulin-conditioned hypoglycemia. This can be explained by the fact that as a result of repeated administrations of insulin, there was a compensatory increase in the functional activity of the adrenal glands. In our experiments we did not obtain condtioned hypoglycemia in a number of dogs. However, it was fully evident after we removed one adrenalin gland and denervated the other.)

Applying a painful stimulus brought about a more rapid coagulation of the blood and an increase in the content of calcium, and prothrombin and in the count of leucocytes and thrombocytes (K. G. Karagezyan). It also produced a number of characteristic shifts in the renal activity, which occur under the influence of pain (G. V. Matinyan, A. S. Oganesyan, G. T. Adunts, and V. B. Yegyan). In using sugar loading as an unconditioned stimulus, we discovered that there was a conditioned increase in the level of glucose and pyruvate in the blood (G. S. Khachatryan).

The results given above and other published data indicate that the cerebral cortex participates extensively in the regulation of the various parts of metabolism. The results obtained in our experiments on developing a cortical inhibition are particularly interesting. This

was achieved through the extinction of the conditioned reflex or through a conditioned inhibition. As the process of inhibition intensified opposite shifts developed. They differed from those observed under the influence of unconditioned or positively conditioned stimuli. Thus for instance, adrenalin-conditioned and dietary hyperglucemia and a conditioned increase in the content of pyruvate. In inhibiting the-adrenalin-conditioned reflex, the quantity of adrenalin-like substances decreased and, in contrast, the quantity of histamine increased. Also, the blood-coagulating time lengthened and the content of potassium, prothrombin, and other ions decreased. A similar mechanism was also observed in other indexes in the inhibition of insulin-conditioned and other reflexes.

Our findings permit us to conclude that in cortical inhibition, on the one hand, the processes reinforced during a cortical irritation become depressed, and, on the other, the opposite processes become activated. Owing to this factor, there is a restoration of substances, the utilization of which involves different manifestations of the irritability of the effector organs. Thus cortical inhibition is of importance not only for the restoration of the brain functioning, but also for other organs necessary to the normal functioning of the brain. The results of our research distinctly confirm I. P. Pavlov's concept of the phenomenon occurring in inhibition, viz., that an active process is concealed behind the mask of a zero effect. This thought can be extended further and the course of its development should be followed up.

The facts stated above indicate that in cortical inhibition, there is an increase in the activity of the opposite functional systems. In a number of cases, this increase was so striking that an unconditioned stimulus (adrenalin, insulin, painful stimulus, sugar loading, etc.), used against the background of inhibition, lost the ability to effect its characteristic influence. In other words, the effect of the first administrations of an unconditioned stimulus was entirely prevented. These data correspond with the results which I. Ye. Perel'-tsveig obtained in I. P. Pavlov's laboratory indicating that there was a considerable weakening in the effect of an unconditioned irritant in inhibition. They also correspond with those of A. O. Dolin, who succeeded in checking the symptoms of morphine intoxication by means of the mechanisms of conditioned inhibition which he developed.

In the process of our experiments, we observed more than once that the effects manifested during a narcotic sleep or cortical inhibition were not similar. We did not detect in the pharmacological sleep (amytal, nembutal) the same symptoms as in the conditioned cortical inhibition (E. Ye. Mkheyan, G. S. Khachatryan).

Having established definite mechanisms in the course of the individual processes of metabolism in the irritation and inhibition of the cortex, we attempted to establish the changes in the absorption of glucose and pyruvate. The latter play an important role in the balance of energy in the cerebral activity of different functions. For the

analysis of the blood we took specimens from the corotid artery of a skin flap and from the external jugular vein. We tied off all the branches of the jugular vein except for the posterior facial vein connected directly with the transverse sinus of the brain. We determined the circulation rate by radioactive phosphorus. Our experiments indicated that in a dietary and dietary-conditioned increase of the glucose and pyruvate content of the blood, the brain intensively absorbs glucose and pyruvate, in spite of the raised circulation rate of the blood. As the process of inhibition intensified, the glucose and pyruvate content of the blood decreased to 40 mg% and 0.2 mg % respectively. At the same time, the arteriovenous difference of glucose disappeared or, in some cases, became negative, and the circulation rate decreased in the brain. In spite of a decrease in the content of pyruvate, the brain continued to absorb it, although insmaller quantities than in the process of irritation. Sugar loading under these conditions produced, as usual, a considerable increase of the content of pyruvate in the blood, with the brain intensively absorbing it. However, the glucose content remained within normal limits, its absorption by the brain was depressed, and the circulation rate remained low. Only 3 or 4 days later could we observe the symptoms characteristic of the effect of sugar saturation. Thus, in inhibiting the conditioned reflex described, the absorption glucose by the brain is depressed even when there is a normal content of sugar in the blood (G. S. Khachatryan).

The data we obtained indicate that there is a considerable activation in the functioning of the insulin apparatus when an alimentary-conditioned hyperglycemia is inhibited. Naturally we became interested in the question of how the absorption of glucose by the brain changes in insulin hypoglycemia. It was found that, in insulin and insulin-conditioned hypoglycemia, the absorption of glucose by the brain was depressed in the majority of cases and that the circulation rate in the brain dropped. The interesting factor was that the brain absorbed pyruvic and lactic acids instead of releasing the latter (V. B. Yegyan and G. S. Khachatryan). It was also interesting to establish the effect of adrenalin hyperglycemia on the same processes as above. In adrenalin hyperglycemia accompnaied by a considerable increase of the pyruvate content in the blood, the absorption of glucose by the brain was reduced in the majority of cases, but pyruvate was fixed in greater quantities than in the control experiments (E. Ye. Mkheyan). Thus, adrenalin hyperglycemia did not produce an increased absorption of glucose by the brain, as it took place in the case of dietary hyperglycemia.

Therefore, various irritants, independently of their effect on the glucose content of the blood, produce an unequal effect on its absorption by the brain. Its absorption is particularly depressed 15 to 20 minutes after an application of a painful stimulus. In a pain or pain-conditioned stimulation accompanied by a slight rise in the glucose content, the absorption of glucose by the brain was particularly strongly depressed 15 to 20 minutes after the action of the stimulus. On the contrary, as the process of inhibition developed, its absorption

increased (V. B. Yegyan, E. Ye. Mkheyan). In this respect, our data did not coincide with those of N. N. Blokhin.

In our experiments we were convinced more than once that in spite of a stimulated condition of the organism, the absorption of glucose by the brain was significantly reduced and that a negative arteriovenous difference was frequently found. We did not observe any particular disturbances in the general behavior of dogs with marked hypoglycemia. In recent years a number of scientists have posed the question of whether glucose is the sole energy material for brain activity (R. Gerard and others). Along this line the experiments of A. Geyger and co-workers, who perfused cats' brains in situ, are of great interest. Starting in 1947, they conducted systematic experiments on cats, perfusing their brain with "simplified blood" (30% erythrocytes, washed out from the blood of cattle, in Krebs-Ringer's solution containing 7% of albumin serum and saturated with 95% oxygen and 5% carbon dioxide). They demonstrated that in such a perfusion, the activity of the brain was maintained to a considerable degree for 4 hours and longer. Normal reflexes of the cornea, the reaction of the pupil to light, normal respiration, blood pressure, and vasomotor functioning, as well as normal electrocorticogram, etc., were all present. Without glucose in the perfusion solution, the activity of the brain continued for over an hour, although glucose disappeared from the brain in 10 or 15 minutes. The addition of matrazol caused spasms and an increased absorption of oxygen by the brain. Under these conditions, the respiratory coefficient fluctuated within the limits of 0.84-0.56, and the content of nucleic acid and, in particular, that of phospholipids decreased in the cerebral cortex and free amino acids were released. On the basis of glucose tagged with carbon, A. Geyger came to the conclusion that in the cerebral tissue a considerable quantity of glucose goes into the formation of amino acids, proteins, lipids, and other acid-insoluble substances which may be utilized in the activity of the brain. The functioning of the brain activated with metrazol increased the disintegration of phospholipids and cerebrosides [see Note].

[Note.] M. Sh. Promyslov also established that there was a decrease in the content of cerebrosides of the brain in tetanus, gas gangrene intoxication, and strychnine effect.

Twenty minutes after spasms, there was an increased synthesis of cerebrosides; their quantity in the cellular layer of the cerebral cortex increased in some cases by 25% in comparison with a quiet period. Stimulation of separate parts of the brain produced an increase of nonprotein nitrogen and a reduction in the nitrogen of nucleic acids and lipids. Although A. Geyger and co-workers did not reproduce in their experiments all the conditions necessary for a normal life activity of the organism, in comparison with other experiments conducted on various brain preparations they are a step ahead. The results obtained merit great attention. They prove that many components of the brain are drawn into the implementation of its activity

Our scientists have also obtained interesting results along this line. We are able to demonstrate in our experiments that in the application of a painful or pain-conditioned stimulus, the brain released in the majority of cases glutinic and aspartic acids, glutamine and glutathione (G. A. Kechek); and that phospholipids and cholesterine were liberated more freely by the brain (K. G. Karagezyan and T. G. Urgandzhyan). The brain released acetylaspartic acid, which is found in considerable quantities in the cerebral tissue. In developing the process of inhibition, opposite manifestations were observed. These were as follows: an increase in the absorption of glutinic and aspartic acids, glutamine and restored glutathione; an obliteration in the arteriovenous differences of phosphates and cholesterine or their absorption by the brain.

The facts given above permit us to conclude that the brain produces an effect on the metabolism of effector organs not only by the nervous mechanism but also by the release of a number of substances into the blood.

The data we obtained indicate that a number of substances are utilized by the cerebral tissue when it is active. Among these substances, glutinic acid, glutamine, and phospholipids are of interest, as is pyruvic acid, which is captured in greater quantities by the brain when its content in the blood is increased. Many scientists consider that glutinic acid may serve as a source of energy in the brain. Its quantity in the brain decreases in insulin hypoglycemia and convulsions caused by various means. When glucose was absent from the culture media, cerebral sections lost glutinic acid. It has been established that before the hematoencephalic barrier develops in babies, glutinic acid penetrates into the brain (H. Himwich) and its content increases. There is a rapid exchange of glutinic acid between the cerebral tissue and the blood of adults, although its level in the brain does not change (H. Welsh and others). The content of glutamine, unlike that of glutinic acid, increases after its introduction. Some authors consider that glutamine is a carrier of glutinic acid (D. V. Tower).

In our experiments on a chloroprene intoxication, we discovered that the cerebral tissue utilizes glutinic and pyruvic acids. A chronic intoxication with chloroprene led to a reduced absorption of glucose in the brain (E. Ye. Mkheyan). The respiration of the cerebral tissue and the activity of a number of ferments, including adenosine, triphosphate, succinic dehydrase, and carbonic anhydrase, became considerably depressed. At the same time, the activity of glutaminoxydase and of pyruvocoxydase greatly increased. An addition of glutinic acid and of pyruvate to the brain homogenates considerably increased the respiration of the cerbral tissue in comparison with the control specimens (V. G. Mkhitaryan).

Concerning the absorption of glucose by the brain, it undergoes changes depending on the specific effect of a stimulus. For this reason, irritation is not always accompanied by an intensive--nor is inhibition accompanied by a reduced--absorption of glucose. The passage of glucose

to the brain is an active process and depends on many factors. This cerebral function is also controlled by the upper sympathetic ganglion. In removing this ganglion in our experiments, there was a considerable depression in the absorption of glucose by the brain. These data are of interest in connection with Ye. A. Astrayan's research establishing that the removal of the upper sympathetic ganglion in dogs disturbed the conditioned-reflex activity.

In spite of the large number of experiments, the functional biochemistry of the brain still remains open to further investigations. This is explained by the intricate structure of the brain, the great sensitivity of this organ to the slightest changes in the environment, and the great variety of metabolic processes securing its important functioning.

(Presented at the Scientific Session, Division of Biological Sciences, Academy of Sciences Armenian SSR, 27 November 1958.)

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